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# Gut

# **Proton pump inhibitors and risk of gastric cancer: population-based cohort study**

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Acid suppressant drugs, which include proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs), are among the most commonly prescribed drugs worldwide. These drugs are used by millions of adults in the United Kingdom (UK) to manage the symptoms of several common gastric conditions, including peptic ulcer disease and gastroesophageal reflux disease. Using the UK Clinical Practice Research Datalink, we conducted a population-based cohort study using a new-user active comparator design to determine whether new users of PPIs are at an increased risk of gastric cancer compared with new users of H2RAs.

With over 1 million patients, followed for a median duration of 5 years, this study was the largest observational study conducted to date on this safety question. Overall, we found that the use of PPIs was associated with a 45% increased risk of gastric cancer. The risk increased with increasing categories of cumulative duration, cumulative dose, and time since treatment initiation. Reassuringly, the number needed to harm was high, with 2121 and 1191 PPI patients followed for five and 10 years after treatment initiation, respectively, to observe one additional gastric cancer case.

Given the pervasiveness of PPIs, physicians should closely monitor their patients to regularly reassess their ongoing need for treatment. In light of the increased risk of gastric cancer, patients who do not have an indication for use should be weaned off their PPI medications.

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